Early-onset Infectious Complications among Penetrating and Severe Closed Traumatic Brain Injury in Active Duty Deployed during OIF and OEF, 2008-2013

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Medical advances in addition to improved body armor during Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) have greatly increased the chance of survival especially among deployment related severe closed and penetrating traumatic brain injury (TBI). However, early medical complications resulting from secondary brain injury play an important role in severe TBI patient outcomes and future survival. Early-onset infectious complications that occurred at a Level IV military treatment facility (MTF) were evaluated among active duty service members that sustained a TBI while deployed during OEF and OIF from calendar years 2008 to 2013. As a group, 14.0% of severe closed and penetrating TBI patients had at least one diagnosis indicating an early-onset infectious complication, most commonly pneumonia followed by systemic infection. However, closed TBI patients developed a greater proportion of early-onset infectious complications compared to penetrating TBI patients. Of infections caused by multidrug-resistant organisms (MDROs), MDR Acinetobacter and MRSA were the predominate pathogens. MDRO infections have the potential to further complicate the care of TBI patients.

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Abstract

Medical advances in addition to improved body armor during Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) have greatly increased the chance of survival especially among deployment related severe closed and penetrating traumatic brain injury (TBI). However, early medical complications resulting from secondary brain injury play an important role in severe TBI patient outcomes and future survival. Early-onset infectious complications that occurred at a Level IV military treatment facility (MTF) were evaluated among active duty service members that sustained a TBI while deployed during OEF and OIF from calendar years 2008 to 2013. As a group, 14.0% of severe closed and penetrating TBI patients had at least one diagnosis indicating an early-onset infectious complication, most commonly pneumonia followed by systemic infection. However, closed TBI patients developed a greater proportion of early-onset infectious complications compared to penetrating TBI patients. Of infections caused by multidrug-resistant organisms (MDROs), MDR *Acinetobacter* and MRSA were the predominate pathogens. MDRO infections have the potential to further complicate the care of TBI patients.

Table of Contents

Abstract ii
Table of Contents iii
Executive Summary 1
Introduction 2
Methods 2
Descriptive Analysis ..... **Error! Bookmark not defined.**
Results 5
Demographic Characteristics 5
Concomitant Injuries 5
Medical Complications 7
Multidrug Resistant Organisms 8
Discussion 9
Limitations 11
References 14
Appendix A 18
Severe Closed TBI ICD-9-CM Diagnosis Codes 18
Penetrating TBI ICD-9-CM Diagnosis Codes 18
Appendix B 19
Multidrug-resistant Organism Definitions 19
Acronym/Abbreviation List 20

Executive Summary

The EpiData Center Department (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) conducts routine surveillance of clinically significant bacterial pathogens and antibiotic resistance patterns within the Department of Defense (DOD). This report provides a summary of early-onset infectious complications that occurred at a Level IV military treatment facility (MTF) among active duty service members who sustained a TBI while deployed during OEF and OIF from calendar years (CY) 2008 to 2013. TBIs are compared according to mechanism of injury (penetrating or severe closed) in the context of selected inherent and acquired medical events that may contribute significantly to infection risk.

The Military Health System's (MHS) databases provide a unique opportunity to investigate the burden of severe TBI and infectious outcomes. To better understand the inherent and acquired medical complications of TBI, particularly as related to early-onset infection, this study aggregates Standard Inpatient Data Record (SIDR) and Theater Medical Data Store (TMDS) TBI records among active duty DOD service members deployed to the OEF and OIF conflicts. In addition, the presence of multidrug-resistant organisms (MDROs) was evaluated using Health Level 7 (HL7) formatted microbiology data. MDRO classification was defined as bacteria resistant to ≥ 3 classes of antibiotics.

As a group, 14.0% of severe closed and penetrating TBI patients had at least one ICD-9-CM diagnosis indicating an early-onset infectious complication, most commonly pneumonia followed by systemic infection. However, closed TBI patients developed a greater proportion of early-onset infectious complications compared to penetrating TBI patients, specifically, pneumonia and systemic infection. Of infections caused by MDROs, MDR *Acinetobacter* and MRSA were the predominate MDROs. Several factors suggest the severity of injury, and thus potential for infection, was greater for closed TBI patients. For instance, the average number of concomitant injures per person and the average number of anatomical locations exposed to concomitant injury were greater for closed TBI patients. The type of injuries for severe closed TBI patients sustained was also suggestive of severe injury. For example, severe closed TBI patients had a greater proportion of internal injuries to the chest and abdomen, traumatic shock, and amputations while penetrating TBI patients experienced more open wounds and fractures to the face.

In the present study, service members who presented with severe closed TBI in addition to internal abdominal and thoracic injury that were in traumatic shock had a greater burden of early-onset infectious complications. Understanding the types of early-onset infectious complications is important for future prevention efforts, as they may serve as reservoirs for late-onset infections. The present study found that more than half of pneumonias were ventilator-associated, suggesting that there are opportunities to improve patient-ventilator management.

Introduction

The Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) conflicts have renewed focus on the importance of traumatic brain injury (TBI) as a source of morbidity among United States (US) active duty military service member both in combat and in routine daily activities in garrison. From 2000 to 2013, the Defense of Veterans Brain Injury Center (DVBIC) reported an estimated 201,778 closed (mild, moderate, severe) and penetrating TBIs among all Department of Defense (DOD) deployed and non-deployed active duty military personnel.[1] Of the total number of TBIs reported the majority were mild, while 10.0% were either moderate, severe or penetrating.

The Veterans Health Administration and Department of Defense (VA/DOD) broadly classify TBI as closed or penetrating.[2] Closed TBIs are usually a result of blunt force trauma that manifests as cerebral contusions and bleeding that occurs inside the skull, but outside the brain. The level of injury severity (mild, moderate, severe) for closed TBIs is based on the level of consciousness, posttraumatic amnesia, neuroimaging, and the Glasgow coma scale (GCS), which measures the amount of central nervous system (CNS) involvement in head injury.[3] In cases of penetrating TBI where the dura mater, the outermost meninges of the brain has been breached; the level of injury stratification is not applied according to the VA/DOD common definition.[2] Both severe closed and penetrating TBIs by nature of the injury are considered potentially life-threatening injuries requiring rapid evacuation to a medical facility that can provide critical care management, including neurosurgical evaluation and intracranial pressure (ICP) monitoring.

The renewed interest in TBI is attributed to reports that service members in OEF and OIF experienced a greater proportion of TBIs compared to previous wars.[3-4] This increase in incidence is in part due to the enemy's heavy use of improvised explosive devices (IEDs), which caused the majority of blast injuries, and the fact that more than 60% of blast injuries resulted in TBIs.[5] Increased survival also influenced TBI incidence, as service members in previous conflicts often did not survive the devastating effects of severe closed and penetrating head injuries. Wars have historically been associated with the development of life-saving medical innovations as evidenced by the substantial increase in the number of wounded per one death.
For instance, the ratio of wounded service members to deceased was 2.3 in World War II, 3.2 in the Vietnam War, and 9.7 in OEF and OIF.[6-7] During OEF and OIF, advances in battlefield medical management, such as far-forward surgical teams, provided life-saving neurological support of severe TBI patients in the form of early in-theater cranial decompression, followed by aggressive critical care management.[8] Medical advances, in addition to improved body armor, greatly increased the chance of survival especially among deployment related severe closed and penetrating TBI patients. A retrospective review of OIF combat causalities, including 408 closed or penetrating TBI cases from 2003-2008 seen for definitive care at Walter Reed Army Medical Center (WRAMC) and National Naval Medical Center (NNMC), concluded that meaningful survival could be potentially achieved in TBI patients presenting with severe disability.[4] However, early medical complications, that result from the ongoing cellular effects of trauma from the primary injury, known as secondary brain injury play an important role in severe closed and penetrating TBI patient outcomes and future survival.[9-11]

Some of the more common early complications that result from secondary brain injury include seizures, hydrocephalus, cerebral spinal fluid (CSF) leaks, infections inside the skull, vascular injuries, and cranial nerve injuries.[9-11] The severity of TBI, in addition to polytrauma, increases the number of and the risk for severe complications.[12] Therefore, the most important goals for medical management of severe closed and penetrating TBIs are to minimize secondary brain injury and prevent infection. With mortality as high as 40% within the first 24 hours after injury, achieving these goals is a delicate balance between neuro-resuscitation and infection prevention.[13]

Penetrating TBI patients are particularly predisposed to intracranial infection due to the nature of injury where a foreign object penetrates the skull and enters the brain. Though lifesaving, extensive use of early decompressive craniectomy performed in the combat theater for both severe closed and penetrating TBI may have equivalently introduced a potential risk for infection for both types of TBI.[9] In addition to the inherent infectious risks of TBI, are the acquired risks that arise from the administration of immunosuppressive drugs, long-term use of antibiotics, decreased host defenses due to poor health status, and presence of invasive devices from medical procedures.[14-17] Identifying ways to prevent or reduce vulnerability to post-injury infection requires an understanding of the epidemiology of injuries, and therefore, requires comprehensive surveillance data.

To better understand the inherent and acquired risks of TBI, as related to early-onset infection, this study aggregates TBI records among active duty DOD service members deployed to the OEF and OIF conflicts from 2008 to 2013. TBIs are compared according to mechanism of injury (severe closed or penetrating) in the context of selected inherent and acquired medical complications that may contribute significantly to infection risk. Characterizing the types and timing of infections can inform the DOD of potential areas wherein improvements in infection screening, diagnosis, and medical care would be of benefit to both personnel and the DOD.

Methods

A retrospective cohort of US active duty military personnel deployed during operations in Afghanistan and Iraq between January 1, 2008 and December 31, 2013 was identified using inpatient and theater medical encounter records available through the Military Health System (MHS). The study population criteria included: a Standard Inpatient Data Record (SIDR) documenting a severe closed or penetrating TBI based on the established DOD TBI case definitions (Appendix A), and a concurrent Theater Medical Data Store (TMDS) record indicating evacuation from theater to a Level IV military treatment facility (MTF) within seven days of injury. SIDR is an electronic database that contains records for direct healthcare inpatient services provided to DOD beneficiaries at fixed MTFs. TMDS is an electronic repository that includes medical encounter records related to in-theater levels of care (I-III). Demographic characteristics, mechanism of injury, concomitant injuries, and medical complications were described using information identified from SIDR. Service branch and active duty status were identified from the patient category. Age was defined as the age at the time of TBI injury using

the TMDS encounter date and the date of birth in SIDR. The military operations in OEF and OIF were classified according to battle casualty locations (Afghanistan and Iraq, respectively). Disposition status was categorized as deceased or living.

The cause of injury was defined by the North Atlantic Treaty Organization (NATO) Standardized Agreement 2050 (STANAG) codes; missing values were categorized as "unspecified." Concomitant injury was evaluated from the injury type and location as defined by ICD-9-CM diagnosis codes in the Barell matrix.[18] Injury type categories (crush, dislocation, sprains/strain, unspecified) had frequencies less than two were classified as "other." Injury location was collated into seven anatomical location categories: head/neck, chest, lower extremity, upper extremity, spine and back, torso, or other. The injury location "other" category included general other and unspecified sites, other multiple sites, and lower extremity unspecified sites. The Barell matrix was not used to identify TBIs, therefore these injuries were excluded from the head injury category when evaluating concomitant injury.

Medical complications were selected according to those that may occur during the acute stage of TBI and polytrauma.[19] Categorization of medical complications was based on the ICD-9-CM diagnosis code multi-level aggregation method developed by the Agency for Healthcare Research and Quality for the Clinical Classifications Software (CCS) tool.[20] Infectious complications were a subset of medical complications grouped by type of infection (systemic, cerebral spinal fluid, pneumonia, fungal, and other bacterial infection). Neurosurgical procedures were based on ICD-9-CM procedure codes used to describe interventions related to severe TBI.[21] The presence of multidrug-resistant organisms (MDROs) in all specimen sources was evaluated using Health Level 7 (HL7) microbiology data. HL7 is a standard messaging format for the transmission of health-related data. Within the MHS, HL7 format is used for the transmission of microbiology, pharmacy, anatomic pathology, chemistry, and radiology data that originates from a fixed MTF's Composite Health Care System (CHCS). Antibiotic susceptibilities were interpreted based on each hospital's entry of certified results into CHCS. MDRO classification was defined as bacteria resistant to ≥ 3 classes of antibiotics (Appendix B).[40] Specimen sources were categorized based on two free text fields that contain the anatomic location and the specimen source (respiratory, skin and soft tissue, blood, medical device, and other unspecified). MDROs identified from the listed specimen sources were considered proxy infections. To establish where the MDRO infections was acquired specimens collected within three days of admission were classified as community-acquired infections and specimens collected on day four or greater of admission were classified as hospital- acquired infections. Groin and external nares are routine sites for active surveillance screening for MDRO colonization at admission for wounded patients from OEF/OIF and these specimen sites were analyzed separately.

Results

Demographic Characteristics

There were 206 patients with penetrating TBI (67.5%) or severe closed TBI (32.5%) that met the study criteria. Table 1 shows selected characteristics for each TBI group admitted to a Level IV MTF following injury during OEF/OIF. The mean evacuation time from theater to the Level IV MTF was slightly greater for closed TBI versus penetrating TBI. Army and Marine Corps service members sustained the majority of TBIs though the frequency between groups did not differ by service branch. Mean age was similar for both groups and males were more likely than females to have experienced either type of TBI. Mortality was similar for both TBI groups during the Level IV admission.

Table 1. Selected Characteristics of Active Duty Service Members Admitted to a Level IV MTF from OEF/OIF with Penetrating or Severe Closed TBI 2008-2013

Characteristic	Penetrating (n = 139)		Closed (n = 67)	
Military Operation, n (%)				
OEF	112	80.6	50	74.6
OIF	27	19.4	17	25.4
Evacuation Time, days				
Mean (SD)[a]	1.3 (0.6)		1.7 (1.1)	
Range	1-3		1-7	
Branch of Service, n (%)				
Army	102	73.4	49	73.1
Air Force	3	2.2	2	3.0
Navy	4	2.9	2	3.0
Marine Corps	30	21.6	14	20.9
Age, years				
Mean (SD)[a]	26.5 (7.2)		25.6 (5.7)	
Range	19-45		19-46	
Gender, n (%)				
Male	139	100	66	98.5
Female	0	--	1	1.5
Disposition Status, n (%)				
Alive	117	84.2	55	82.1
Deceased	22	15.8	12	17.9

Cells with "--" indicate no value for the category.

[a] SD = standard deviation

Data are from Standard Inpatient Data Record (SIDR) and Theater Medical Data Repository (TMDS).

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Concomitant Injuries

The cause of injury varied by TBI group ($p < 0.0001$) (Table 2). Blasts were the leading cause of injury for both TBI groups followed by gunshot wounds, although the percentage of these two causative agents was higher among penetrating TBI patients. Patients with closed TBIs experienced a higher proportion of motor vehicle accidents. The percentage of patients that sustained concomitant injury did not differ by TBI group (penetrating TBI n=112, 80.6% vs. closed TBI n=60, 89.6%; $p = 0.10$). However, the average number of injures per person was

greater for closed TBIs than for penetrating TBIs (closed: mean 5.1; penetrating: mean 4.2 p = 0.05).

Of the anatomical locations compared between TBI groups, only the percentages of chest, spine, and torso injuries were significantly higher among closed TBI patients than for penetrating TBI patients) (Table 2). On average, patients with closed TBIs also had a greater number of anatomical locations exposed to injury. Among the injury types sustained, open wounds were significantly more frequent among penetrating TBIs (p = 0.01) whereas closed TBIs suffered a significantly greater percentage of internal injuries, system wide injuries, and amputations.

Table 2. Selected Characteristics of Active Duty Service Members Admitted to a Level IV MTF from OEF/OIF with Pentrating or Severe Closed TBI, 2008-2013

Characteristic	Penetrating (N =139)		Closed (N = 67)		*p*
Mechanism of Injury, n (%)					<0.0001
Blast	90	64.7	40	59.7	
Gunshot wound	41	29.5	9	13.4	
Motor vehicle accident	2	1.4	8	11.9	
Aircraft accident	1	0.7	2	3.0	
Other accidents	2	1.4	5	7.5	
Unspecified	3	2.2	3	4.5	
Concomitant Injury by Location, n (%)					
Head/neck	91	65.5	38	56.7	0.22
Chest	29	20.9	34	50.7	<0.0001
Lower extremity	50	36.0	34	50.7	0.13
Upper extremity	58	41.7	29	43.3	0.67
Spine and back	15	10.8	27	40.3	<0.0001
Torso	20	14.4	31	46.3	<0.0001
Other	27	19.4	22	32.8	0.08
Concomitant Injury by Type, n (%)					
Open wound	84	60.4	34	50.7	0.01
Fracture	77	55.4	49	73.1	0.07
Burn	9	6.5	3	4.5	0.55
Internal	25	18.0	34	50.7	<0.0001
Contusion/superficial	16	11.5	7	10.4	0.63
Systemwide	18	12.9	19	28.4	0.02
Amputation	9	6.5	15	22.4	0.02
Nerve	8	5.8	3	4.5	0.75
Blood vessel	7	5.0	2	3.0	0.50
Other	5	3.6	5	7.5	0.32

Data are from Standard Inpatient Data Record (SIDR) and Theater Medical Data Repository (TMDS).
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Medical Complications

As shown in Table 3, the average length of hospital stay (LOS) was significantly greater for patients with closed TBIs than for patients with penetrating TBIs ($p = 0.04$). During admission, penetrating TBI cases had a higher proportion of documented neurosurgical procedures compared to closed TBI cases (30.9% vs. 16.4%, respectively; $p = 0.03$). Penetrating TBI cases were more likely to have intracranial pressure (ICP) monitoring, brain debridement, and brain repairs, whereas closed TBI cases underwent a greater percentage of ventriculostomy replacement/removals. However, there were no statistically significant differences in the percentage of neurological procedures between the two TBI groups.

Both TBI groups experienced at least one of the selected acute medical complications related to TBI and polytrauma with similar frequency (penetrating 76.4% vs. closed 77.6%; $p = 0.83$). The average number of selected medical complications per person did not vary by TBI group (penetrating TBI: mean 3.1, closed TBI: mean 2.9; $p = 0.66$). However, closed TBI patients were significantly more likely than penetrating TBI patients to have anoxic brain damage (coma, stupor, brain damage category) (11.9% vs. 1.4%, respectively; $p = 0.004$) and infections (26.9% vs. 7.9%, respectively; $p = 0.0002$). Stratification of patients with infectious complications identified from documented ICD-9-CM diagnosis codes showed that closed TBI patients developed a greater percentage of systemic infections and pneumonia compared to penetrating TBI patients. Of the cumulative number of pneumonia cases that occurred among both TBI groups, 13 (52.0%) were ventilator-related.

Table 3. Selected Characteristics of Active Duty Service Members Admitted to a Level IV MTF from OEF/OIF with Pentrating or Severe Closed TBI, 2008-2013

Characteristic	Penetrating (N =139)		Closed (N = 67)		*p*
Length of Hospital Stay, days					
Mean (SD)[a]	3.1 (2.4)		4.1 (3.3)		0.04
Range	1-14		1-16		
Neurosurgical Procedures, n (%)					
ICP monitoring	32	23.0	9	13.4	0.11
Craniotomy/Craniectomy	15	10.8	7	10.4	0.70
Brain debridement	15	10.8	2	3.0	0.06
Brain repair	9	6.5	1	1.5	0.09
Ventriculostomy replace/remove	13	9.4	7	10.4	0.80
Medical Complications, n (%)					
Acute posthemorrhagic anemia	78	56.1	32	47.8	0.55
Coagulation and hemorrhagic	32	23.0	11	16.4	0.38
Coma, stupor, and brain damage	2	1.4	8	11.9	0.004
Seizure	2	1.4	3	4.5	0.33
Occlusion of cerebral arteries	3	2.2	2	3.0	0.66
Central nervous system	55	39.6	27	40.3	0.93
Respiratory insufficiency/failure	46	33.1	32	47.8	0.17
Fluid and electrolyte	24	17.3	12	17.9	0.91
Venous embolism/thrombosis	6	4.3	4	6.0	0.73
Infection	11	7.9	18	26.9	0.0002
Infectious Complications, n (%)					
Systemic	2	1.4	6	9.0	0.02
Meningitis	1	0.7	1	1.5	0.55
Pneumonia	9	6.5	13	19.4	0.03
Fungal	2	1.4	2	3.0	0.60

[a] SD = standard deviation

Data are from Standard Inpatient Data Record (SIDR) and Theater Medical Data Repository (TMDS).

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Multidrug Resistant Organisms

Fifty-two (25%) TBI patients were culture positive for an MDRO during the Level IV admission (Table 4). Of the total number of MDROs identified, twenty-nine (55.8%) were considered a proxy infection and the majority of these samples (91%) were collected within the first three days of admission. Approximately 44.2% of the MDROs were active surveillance samples collected within the first two days of admission as per MTF protocol.

Among proxy infection samples, respiratory specimens predominated for both TBI groups; however, the identified MDRO varied (penetrating TBI: MDR *Acinetobacter* species vs. closed TBI: Methicillin-resistant *Staphylococcus aureus*). Extended-spectrum beta lactamase *Escherichia coli* (ESBL *E. coli*) was the most frequently identified MDRO (n=18; 78.2%) among active surveillance samples. All surveillance samples were collected from the groin.

Table 4. Number of Multidrug Resistant Organisms by Specimen Source among Penetrating and Severe Closed TBI, 2008-2013

Penetrating TBI

MDRO	Specimen Source						
	Surveillance	Respiratory	SSTI[a]	Blood	Device	Other	Total
ESBL *E. coli*	9	2	0	0	0	1	12
MDR *Acinetobacter* species	2	4	0	0	0	0	6
MRSA	0	2	0	0	0	0	2
ESBL *Enterobacter* species	1	0	0	0	0	0	1
ESBL *Klebsiella pneumoniae*	0	0	0	1	0	0	1
Total	12	8	0	1	0	1	22

Severe Closed TBI

MDRO	Specimen Source						
	Surveillance	Respiratory	SSTI[a]	Blood	Device	Other	Total
ESBL *E. coli*	9	0	2	1	0	0	12
MDR *Acinetobacter* species	1	3	2	0	0	0	6
MRSA	0	6	1	0	0	0	7
ESBL *Enterobacter* species	1	1	0	0	1	0	3
ESBL *Klebsiella pneumoniae*	0	1	0	0	0	0	1
MDR *Streptococcus pneumoniae*	0	1	0	0	0	0	1
Total	11	12	5	1	1	0	30

[a] SSTI = skin and soft tissue infection

Data are from NMCPHC HL7 microbiology.

Prepared by the EpiData Center Department, Navy Marine Corps Public Health Center, September 2014.

Discussion

This study described early-onset infectious complications among active duty service members with deployment-related severe closed and penetrating TBI. Assessment was limited to the initial Level IV admission to characterize early-onset infectious complications that may provide insight into understanding potential reservoirs of infection that predominate at this level of care. These results may have implications for prevention efforts as patients move through levels of medical care, from Levels I to III in-theater, to Level IV outside the combat zone, and then to Level V in the continental US.

As a group, 14.0% of penetrating and severe closed TBI patients had at least one ICD-9-CM diagnosis indicating an early-onset infectious complication. However, closed TBI patients developed a greater proportion of early-onset infectious complications compared to penetrating TBI patients specifically, pneumonia and systemic infection. Several factors suggest the severity of injury, and thus potential for infection, was greater for closed TBI patients. For example, the average number of concomitant injures per person and the average number of anatomical locations exposed to concomitant injury were greater for closed TBI patients. The types of injuries for closed TBI patients sustained was also suggestive of severe injury. For instance, closed TBI patients had a greater proportion of internal injuries to the chest and abdomen, traumatic shock, and amputations while penetrating TBI patients experienced more open wounds and fractures to the face. In a study of critical care trauma patients, traumatic shock was the only admission characteristic associated with infection, and infection developed faster in these patients compared to patients without shock.[22] Several studies have established that internal injuries of the thoracic and abdominal cavity are associated with high mortality and of patients

that survive, infectious complications are common. [23-28]

The finding that pneumonia was an early-onset infectious complication is consistent with studies in trauma patients where the median time to infection was 3-5 days.[20,21,25,27] Pneumonia is a common complication of severe brain injury due to the patient's decreased level of consciousness, aspiration of secretions, inability to protect the airway, and decreased mobility. Consequently, early-onset systemic infection was found to occur in trauma patients with pulmonary contusion and abdominal and torso injuries.[25-28] In addition, pneumonia often preceded systemic infection.

Among all TBI patients in the present study, posttraumatic meningitis was less than 1.0%. However, from the time of injury, posttraumatic meningitis can range from 24 hours to years with a median of 5-13 days.[29-30] Accordingly, the posttraumatic meningitis incidence of 9.1% reported among closed and penetrating TBI patients presenting to WRAMC and NNMC from 2003-2008 supports the likely influence that short length of stay (3-4 days) had on incidence in the present study. Post-traumatic meningitis incidence may also be influenced by the evolution of TBI management strategies. During OEF/OIF, the DOD implemented modifications to the strategies used in previous military conflicts to prevent secondary brain injury in penetrating and closed head trauma. Older methods used aggressive debridement, which the MHS abandoned after the connection between infection and worsened outcomes was made.[9] The new standard is aggressive decompression with subsequent watertight dural closure which is done to reduce CSF leaks and meningitis.

MDR *Acinetobacter* and MRSA were the predominate MDROs isolated from respiratory samples. Most microbiology samples with an MDRO identified were collected before the third day of admission. The finding suggests that MDRO acquisition was related to exposures nearer the time of injury and/or during medical evacuation rather than exposures in the Level IV hospital environment. This observation is commensurate with a study of combat-related injuries and infection epidemiology.[32] ESBL *E. coli* detected through active surveillance cultures in the present study was also consistent with results from studies in similar patient populations.[31-33] In retrospect, standardized infection control and prevention efforts evolved throughout OIF/OEF as the source and extent of MDR infection/colonization among war wounded service members became known. The uniform implementation of admission surveillance for MDRO colonization in 2009 became one of the most effective interventions to track and prevent MDROs in this population. However, the MDRO issue emphasizes the need for comprehensive surveillance systems to monitor infectious disease enterprise-wide.

Infectious complications are often an underreported and under recognized cause of morbidity in civilian trauma patients.[22] However, the recent military conflicts in OEF/OIF have renewed focus on infections among service members with combat-related injuries. This is evidenced by Clinical Practice Guidelines (CPG) developed first in 2008 and updated in 2011 to provide recommendations for injury-specific antimicrobial prophylaxis specifically from the time of injury in the combat zone to Level IV facilities.[34,35] A recent study on CPG adherence found that although improvements were made for each injury pattern in comparison to the previous

evaluation (current analysis 60% to 83% versus 10% to 79% in the previous analysis), there was still need for improvement.[36] The extent to which the CPG influenced the present study outcome of early-onset infectious complications is uncertain.

Several studies have emphasized the role infection has in determining patient outcomes.[17,22,30] Therefore, establishing which groups are at risk of developing early-onset infectious complications may lead to better risk stratification and therapeutic approaches. In the present study, patients who presented with severe closed TBI in addition to internal abdominal and thoracic injury that were in traumatic shock had a greater burden of early-onset infectious complications. This suggests that differences in the number and severity of extracranial concomitant injuries between closed and penetrating TBI patients in this cohort of OIF/OEF service members may have influenced the risk of infectious complications more significantly than merely the type of TBI. Thus, early diagnosis and implementation of specific infection management protocols for severe concomitant injuries may not only improve the functional gains among TBI patients, but also contribute to the reduction of infection risk. In addition, identifying the types of early-onset infectious complications is important for future prevention efforts as they may serve as reservoirs for late-onset infections. For example, the present study found that 59% of pneumonias were ventilator-associated, suggesting that there are opportunities to improve patient-ventilator management.

It is important to note that the present study represents infection burden among TBI patients that were admitted at a Level IV MTF long enough to develop early-onset infectious complications as patients had varying lengths of stay. Therefore, it is likely that the study results underestimate early-onset infections. However, the study results are consistent with previous studies that report patients with the most severe injuries, specifically abdominal and thoracic injuries and traumatic shock are likely to develop early-onset infectious complications.[21,24,25]

Limitations

The present study includes severe closed and penetrating TBI service members that survived injury in the OEF/OIF theaters of operation and evacuation to Level IV medical care. Service members must meet specific medical requirements to deploy and thus represent an overall healthy population. In addition, the type of combat weaponry influences the range of traumatic injuries that are sustained during military conflicts. As weaponry continues to evolve, so too may the types of traumatic injuries and risk of infectious complications that present for medical care. Therefore, given these factors, the results in the present study may not be generalizable.

Data for the study were collected retrospectively and are dependent on the accuracy of the ICD-9-CM diagnosis codes in SIDR. Sixteen percent of patients had an isolated TBI, meaning the severe closed or penetrating TBI patient sustained no concomitant injury. Isolated TBIs among combat-related injury have been reported.[21] Therefore, this 16% in the present study could truly be the proportion of patients that had isolated TBIs or represent incomplete ICD-9-CM diagnosis coding.

HL7 formatted data were generated within the CHCS at fixed MTFs. Microbiology data were used to confirm the etiologic agent for infection or colonization. However, the microbiology data does not capture cases in which a physician chooses to treat presumptively without laboratory confirmation. The extent to which patients were presumptively treated for infection in the present study is unknown. Hence, any presumptive treatment will have led to underestimates of infectious complications.

The use of microbiology data for analysis of antibiotic resistance is limited by the practice of cascade reporting, where antibiotic sensitivity results are conditionally reported to CHCS to guide treatment decisions. DOD MTFs practice cascade reporting to varying degrees. Furthermore, not all laboratories in the DOD operate under the same version of Clinical Laboratory Standards Institute (CLSI) guidelines. As a result, certain facilities use guidelines with outdated antibiotic susceptibility breakpoints and may incorrectly report some susceptibilities. Thus, the burden of MDROs in the present study may be underestimated.

The Barell matrix is a basic tool that standardizes the characterization of patterns of injury by type and location using ICD-9-CM diagnosis codes. The matrix has been used in injury surveillance for case mix comparisons over time and place. However, the matrix in its original conceptual development was not intended to measure injury severity. Clark and Ahmad developed a method to estimate injury severity using the Barell matrix, but a literature search revealed no journal articles that report using the referenced study's methods.[38] In the present study, infectious complications for each TBI group are described in the context of basic comparisons of the nature of injury, location, and number of injuries with no intention of purporting the measures as actual estimates of injury severity.

The Barell two-dimensional matrix classifies injury by type and body region. "Systemwide" injuries are not two-dimensional. The Barell matrix utilizes International Classification of

Disease-9th Revision Clinical Modification (ICD-9-CM) codes ranging from: 800 to 995.85.: injuries and poisonings excluding complications of surgical and medical care and does not include ICD-9-CM codes intended to capture external cause of injury ("E-codes"). Injuries that are not covered under the Department of Defense (DOD) injury prevention programs, like injuries that are the result of physical or criminal abuse, are excluded from EDC reports.

Many cells in the Barell matrix are defined by more than one ICD-9-CM code; therefore, injuries of the same type and location may not be identical in nature nor in severity. The Barell matrix does not assign injury severity. Barell-identified injuries are subject to the vagaries of ICD-9-CM codes, which do not differentiate between left and right (e.g., extremities), and may not precisely define the body site of an injury. The three categories of Traumatic Brain Injury (TBI) identified by the Barell matrix do not meet the standard definition of TBI used by the EDC; however, they are head injuries. However, the Barrell matrix was not used to identify TBI in the present study.

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Appendix A

Severe Closed TBI ICD-9-CM Diagnosis Codes

800.04	800.14	800.24	800.34	800.44	800.54	801.04	801.14	801.24
801.34	801.44	801.54	803.04	803.14	803.24	803.34	803.44	803.54
804.04	804.24	804.34	804.34	804.44	804.54	850.30	851.04	851.24
851.44	851.64	851.84	852.04	85224	852.44	852.44	854.04	80015
800.25	800.35	800.45	800.55	801.05	801.13	803.61	800.62	800.72
801.15	80125	801.35	801.45	801.55	803.05	803.15	803.25	803.35
803.45	80355	80405	804.25	804.35	804.35	804.45	804.55	850.40
851.05	851.25	851.45	851.65	851.85	852.05	852.25	852.45	800.82
852.45	854.05	853.05	800.53	800.63	800.73	800.83	800.93	801.03
800.92	803.62							

Penetrating TBI ICD-9-CM Diagnosis Codes

800.61	800.71	800.81	800.91	801.61	801.71	801.81	801.91
803.61	803.71	803.81	803.91	804.61	804.71	804.81	804.91
851.11	851.31	851.51	851.71	851.91	852.11	85231	852.51
852.71	852.91	853.11	854.11	800.62	800.72	800.82	800.92
801.62	801.72	801.82	801.92	803.62	803.72	803.82	803.92
804.62	804.72	804.82	804.92	851.12	851.32	851.52	851.72
851.92	852.12	852.32	852.52	852.72	852.92	853.12	854.12
800.63	800.73	800.83	800.93	801.63	801.73	801.83	801.94
803.63	803.73	803.83	803.94	804.63	804.73	804.83	804.93
851.13	851.33	851.53	851.73	851.93	852.13	852.33	852.53
852.73	852.93	853.13	854.13	800.74	800.84	800.94	800.64
801.64	801.74	80184	801.94	803.64	803.74	803.84	803.94
804.64	804.74	804.84	804.94	851.14	851.34	851.54	851.74
851.94	852.14	852.34	852.54	852.74	852.94	853.14	85414
800.65	800.75	800.85	800.95	801.65	801.75	801.85	801.95
803.65	803.75	803.85	803.95	80365	803.75	803.85	803.95
804.65	804.75	804.85	804.5	851.15	85135	851.55	851.75
851.95	852.15	852.35	85255	852.75	852.95	853.15	854.15
800.60	800.66	800.69	800.70	800.76	800.79	800.80	800.86
800.89	800.90	800.96	800.99	801.60	801.66	801.69	801.70
801.76	801.79	801.80	801.86	801.89	801.90	80196	801.99
804.70	803.60	803.66	803.69	803.70	803.76	803.79	803.80
803.86	803.89	803.90	803.96	803.99	804.60	804.86	804.89
804.96	804.99	851.10	851.16	851.19	851.30	851.36	851.39
851.50	851.56	851.59	851.70	851.76	851.79	851.90	851.96
851.99	852.10	85216	85219	852.30	852.36	852.39	852.50
852.59	852.70	852.76	852.79	852.90	852.96	852.99	804.90
853.10	853.16	853.19	854.10	854.16	854.19	852.56	

Appendix B

Multidrug-resistant Organism Definitions

Methicillin-resistant *Staphylococcus aureus* (MRSA)	Resistant to oxacillin.
Vancomycin-resistant *Enterococcus* (VRE)	Resistant to vancomycin.
Extended spectrum beta-lactamase (ESBL) *Escherichia coli*	Resistant to one of the following: cefepime, ceftazidime, ceftriaxone, cefotaxime, aztreonam, cefixime.
Extended spectrum beta-lactamase (ESBL) *Klebsiella pneumoniae*	Resistant to one of the following: cefepime, ceftazidime, ceftriaxone, cefotaxime, aztreonam, cefixime.
Multidrug-resistant (MDR) *Acinetobacter baumannii*	Non-susceptible to at least one agent from at least three of the following classes: aminoglycosides, antipseudomonal carbapenems, antipseudomonal fluoroquinolones, antipseudomonal penicillins+inhibitors, extended spectrum cephalosporins, folate pathway inhibitors, monobactams, penicillins+inhibitors, polymyxins, tetracyclines.
Multidrug-resistant (MDR) *Pseudomonas aeruginosa*	Non-susceptible to at least one agent from at least three of the following classes: aminoglycosides, antipseudomonal carbapenems, antipseudomonal cephalosporins, antipseudomonal fluoroquinolones, antipseudomonal penicillins+inhibitors, monobactams, phosphonic acids, polymyxins.
Multidrug-resistant (MDR) *Streptococcus pneumoniae*	Resistant to penicillin and at least two other non-beta-lactamase antibiotics.

Acronym/Abbreviation List

Acronym/Abbreviation	Definition
AD	Active duty
CHCS	Composite Health Care System
CCS	Clinical Classifications Software
CLSI	Clinical Laboratory Standards Institute
CPG	Clinical Practice Guidelines
CY	Calendar year
DVBIC	Defense of Veterans Brain Injury Center
DOD	Department of Defense
EDC	EpiData Center Department
ESBL	Extended-spectrum beta lactamase
HL7	Health Level 7
ICP	Intracranial pressure
ICD-9-CM	International Classification of Disease, Ninth Revision, Clinical Modification
LOC	Loss of consciousness
LOS	Length of hospital stay
MDRO	Multidrug-resistant organisms
MHS	Military Health System
MRSA	Methicillin-resistant Staphylococcus aureus
MTF	Military Treatment Facility
NATO	North Atlantic Treaty Organization
NNMC	National Naval Medical Center
NMCPHC	Navy and Marine Corps Public Health Center
OCONUS	Outside of the continental United States
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
SIDR	Standard Inpatient Data Record
STANAG	Standardized Agreement
TBI	Traumatic Brain Injury
TMDS	Theater Medical Data Store
US	United States
WRAMC	Walter Reed Army Medical Center